

REMARKS

Status of the Claims

Claims 1-8, 10-27, 29-39, and 87-89 are pending. Claims 23, 24, 29, 33 and 36 are amended. Claims 26 and 34 are canceled in the amendment.

Claims 1-8, 10-22, and 39 are allowed. Claims 23-27, 29-33, 35, 36, and 87-89 are rejected. Claims 28, 37, and 38 are objected to as being dependent on a rejected claim. Claim 34 is believed to be objected to as well.

Issues Under 35 U.S.C. § 112, second paragraph

Claims 23-27, 29-32, 36, and 87-89 stand rejected under 35 U.S.C. § 112, second paragraph as allegedly being indefinite. This rejection is respectfully traversed. However, the above amendments are believed to render this rejection moot.

Above, Claim 36 is amended to be dependent on claim 35.

Claim 23 is amended to recite “a subject” and is directed to a method of “analyzing” an activity of COX-2”.

Claims 24 and 25 clearly relate back to amended claim 23.

Claim 29 is amended to further feature the detecting step.

Accordingly, the Examiner is respectfully requested to withdraw this rejection.

Issues Under 35 U.S.C. § 112, first paragraph

Claims 23-25, 29-33, 35, 36, and 87-80 stand rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the written description requirement. Additionally, claims 23 and 32 are rejected under 35 U.S.C. § 112, first paragraph, as allegedly not being enabled.

These rejections are respectfully traversed. Reconsideration and withdrawal thereof are requested.

Although traversed by Applicants, the rejection of claims 23-25, 29-33, 35, 36, and 87-80 above is moot in view of the above amendment. Claims 23 and 33 are amended to include a feature of claims 26 and 34, respectively. Claims 26 and 34 are free from this rejection and such amendment should overcome this rejection.

With respect to the enablement rejection of claims 23 and 32, the Office Action alleges that “[w]ithout specific teachings in the specification, one of skill in the art would reasonable [sic] conclude that the expression of COX-2 in pathological tissue in vivo would not have a nexus to the expression of COX-2 in a cell adapted to tissue culture conditions.”

The Examiner’s attention is respectfully directed to the specification, where culture conditions are mentioned throughout. For example see page 30, lines 11-13: “Treatment with a selective COX-2 inhibitor reduced tumor formation by 85 to 90 percent and inhibited colony formation of cultured cells (Sheng, H, *et al.* 1997, *J. Clin. Invest.* 99:2254).”

Additionally, see the specification at page 31, lines 16-22.

Significantly, Example 8, in the specification on page 40-41 demonstrates how samples may be “collected from or prepared from cultured cells.” Additionally, Example 11 in the

specification (page 43-44) discusses the direct quantification of COX-2 activity from *in vitro* examples. Accordingly, the Specification has a more than adequate “teachings” sought by the Examiner.

The test for enablement is whether one reasonably skilled in the art could make or use the invention from the disclosures in the patent coupled with information known in the art without undue experimentation. *United States v. Teletronics, Inc.*, 8 U.S.P.Q.2d 1217, 1223 (Fed. Cir. 1988). The fact that experimentation may be complex does not necessarily make it undue, if the art typically engages in such experimentation. *Massachusetts Institute of Technology v. A.B. Fortia*, 227 U.S.P.Q. 428 (Fed. Cir. 1985). Additionally, the Examiner has the burden to establish a reasonable basis to question the enablement provided in the claimed invention. M.P.E.P. § 2164.04. Applicants respectfully submit that the Office Action fails to present a reasonable basis to question enablement. There is considerable direction and guidance in the Specification, and all of the methods needed to practice the invention are well known.

The Office Action cites a portion of The Culture of Animal Cells to support the notion that “pathological tissue taken from a patient suffering from a COX-2 related disorder would persist in expressing COX-2 when grown as a cultured cell.” See the Office Action at page 6. However, the cited text, a portion of a chapter entitled “Culture of Tumor Tissue,” is overly general and fails to offer any evidence that a model directed to COX-2 expression is even relevant to the discussion.

As stated in M.P.E.P. § 2164.02:

Since the initial burden is on the examiner to give reasons for the lack of enablement, the examiner must also give reasons for a conclusion of lack of correlation for an *in vitro* or *in vivo* animal model example. A rigorous or an invariable exact correlation is not

required, as stated in *Cross v. Iizuka*, 224 U.S.P.Q. 739, 747 (Fed. Dir. 1985) (emphasis added).

Additionally, the Journal of Biological Chemistry article cited in support of the rejection was co-authored by the instant inventors. That paper discussed exogenous 2-AG metabolism and endogenous 2-AG production and metabolism by RAW264.7 cells grown in DMEM, the same cells discussed in Example 8 of the instant specification.

In summary, the arguments with respect to the cultured cell issues are conclusory, and applicants respectfully submit that the evidence does not support the conclusion that one of ordinary skill in the art would not be able to make or use the present invention without undue experimentation.

Issues Under 35 U.S.C. § 102

Claims 33, 35, and 36 are rejected under 35 U.S.C. § 102 (b) as allegedly being anticipated by Yu et al., Journal of Biological Chemistry, 1997, Vol 272, pp. 21181-21186. This rejection is respectfully traversed. However, in view of the above amendment, this rejection is believed to be moot. As stated above, claim 34 as been incorporated into claim 33. Claim 34 is free from this rejection.

Issues Under 35 U.S.C. § 103

Claim 23-25, 29-32, and 87-89 stand rejected under 35 U.S.C. § 103 as allegedly being obvious over Isakson et al. (WO 97/14679), in view of the Yu et al. article. This rejection is respectfully traversed. However, this rejection is moot in view of the above amendment. As

stated above, claim 26 is incorporated into claim 23. Claim 26 is free from this rejection.

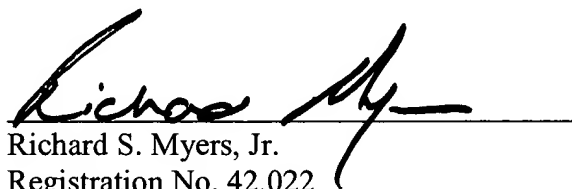
Accordingly, in view of the amendment, this rejection should be withdrawn.

From the foregoing, further and favorable reconsideration in the form of a Notice of Allowance is believed to be in order and such action is earnestly solicited.

Pursuant to 37 C.F.R. §§ 1.17 and 1.136(a), Applicants hereby petition for a two-month extension of time for filing a response. The fee of \$ 225 is being filed herewith. The Commissioner is requested to charge any deficiency and credit any overpayment related to this or future to deposit account number 50-2752.

If the Examiner has any questions concerning this election or the Application in general, she is respectfully requested to contact the undersigned at the number listed below.

Respectfully submitted,

A handwritten signature in black ink, appearing to read "Richard S. Myers, Jr.", is written over a horizontal line.

Richard S. Myers, Jr.
Registration No. 42,022
STITES & HARBISON, PLLC
Customer No. 32885
424 Church Street, Suite 1800
Nashville, TN 37219
(615) 782-2333

Attorneys for Applicant